

R E M A R K S

The Office Action dated April 16, 2003 presents the examination of claims 2, 4, 6, 8, 14, and 25. Claims 9-11 and 15-24 remain withdrawn from consideration. Claims 9 and 14-24 are canceled herein. Claims 2, 4, and 12 are amended. Support for the addition of "of 8-14 amino acids in length" to claims 2 and 4 is found in the specification on page 13, line 4. Claim 12 is amended to update claim dependency. Upon entry of this Reply, claims 2, 4, 6, 8, 10-12, and 25 will be pending. No new matter is inserted into the application.

Request for Initialed Form PTO-1449

Applicants filed an Information Disclosure Statement (IDS) on December 22, 2000. The Examiner has not yet acknowledged the references contained in this IDS. The Examiner is respectfully requested to consider these references, and initial and return the Form PTO-1449 as evidence of her consideration thereof. A copy of the Form PTO-1449 is attached hereto for the Examiner's convenience.

A second Form PTO-1449 corresponding to an IDS filed on June 21, 2002 was attached to the Office Action dated April 16, 2003. However, the Examiner did not initial three of the five references listed on this Form PTO-1449. No reason is given in the Office Action for why these references are not initialed.

The Examiner is respectfully requested to consider these references, and initial and return the Form PTO-1449 as evidence of her consideration thereof. A copy of the Form PTO-1449 is attached hereto for the Examiner's convenience.

Restriction Requirement

The Examiner maintains the withdrawal of claims 15-24 from further consideration for being drawn to a non-elected invention. Claims 15-24 are canceled, thus rendering the restriction moot.

The Examiner also maintains the withdrawal of claims 9-11 from consideration for allegedly being drawn to a non-elected species. Claim 9 is canceled, thus rendering the restriction thereof moot. However, Applicants respectfully traverse the withdrawal of claims 10 and 11, and request rejoinder thereof with the examined claims.

Specifically, claims 10 and 11 depend from elected claim 8. Claim 10 recites SEQ ID NO: 38, which is a derivative of elected species SEQ ID NO: 2. Claim 11 recites SEQ ID NO: 40 which is also a derivative of elected species SEQ ID NO: 2. Since the Examiner has already searched and considered SEQ ID NO: 2, no undue burden would be placed on the Examiner to consider derivatives thereof.

For this reason, Applicants respectfully request that the Examiner withdraw the restriction requirement, and examine claims 10 and 11 on their merits.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner maintains the rejection of claim 14 under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter not enabled by the specification. Claim 14 is canceled, thus rendering the rejection moot.

Rejection under 35 U.S.C. § 102

The Examiner maintains the rejection of claims 2, 4, 6, 8, 12, and 25 under 35 U.S.C. § 102(b) for allegedly being anticipated by Price (1991). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Price discloses the amino acid sequence of cyclophilin B. However, Price fails to disclose an isolated tumor antigen peptide of 8-14 amino acids in length that binds to an HLA antigen and is recognized by cytotoxic T lymphocytes.

As noted above, Price discloses the cyclophilin B protein. However, the entire sequence disclosed by Price not would bind to HLA antigen and be recognized by CTL. For example, only small peptides, i.e. peptides of between 8 and 14 amino acids, are

capable of binding HLA antigen. This feature of peptides is described on page 13, line 3-4 of the specification, and recited in the instant claims. Therefore, the entire sequence as disclosed by Price would not bind HLA antigen and would not be recognized by CTL.

On pages 3-4 of the Office Action, the Examiner argues that the protein disclosed by Price would "inherently" bind HLA antigen and be recognized by CTL. Applicants respectfully disagree.

The Examiner has not shifted the burden to Applicants

It is respectfully submitted that the burden is on the Examiner in the first instance to demonstrate that the prior art inherently possesses the claimed features. "Once a reference teaching a product appearing to be substantially identical is made the basis of a rejection, and the Examiner presents evidence or reasoning tending to show inherency, the burden shifts to the Applicant to show an unobvious difference." U.S. Pat. & Trademark Off., Manual Pat. Examining Proc. § 2112 (8th ed. 2001) (emphasis added). In the instant case, the Examiner has failed to present evidence or reasoning tending to show that the protein disclosed by Price would inherently bind HLA antigen and be recognized by CTL.

In making the "inherency" rejection over Price, the Examiner states,

"Applicant argues that Price et al do not teach each and every limitation of instantly claimed invention, i.e. Price et al do not disclose an isolate tumor antigen peptide that binds to an HLA antigen and is recognized by CTL. The argument is not commensurate with the scope of claims because the instant invention is drawn to peptide **comprising** SEQ ID NO:2 and Price et al teach peptide comprising the instant SEQ ID NO:2 at Fig. 1 at page 1904. Note that instant SEQ ID NO:2 is identical to amino acid #91-99 of the protein at Fig. 1 of Price et al. Although Price et al do not teach the peptide sequence amino acid #91-99 of the protein at Fig. 1 binds to HLA and recognized by CTL, those are the inherent properties of the protein comprising the peptide." (Emphasis in original).

Nowhere in this recitation does the Examiner present evidence or reasoning tending to show that the protein disclosed by Price would bind HLA antigen and be recognized by CTL.

MPEP § 2112 states that once the Office has established substantial similarity and the Examiner presents evidence or reasoning tending to show inherency, the burden shifts to Applicants to show an unobvious difference. However, the Examiner is missing an essential piece of the rejection. Again, nowhere in the rejection has the Examiner provided evidence or reasoning, either implicit or explicit, tending to show that the protein disclosed by Price would bind HLA antigen and be recognized by CTL. "In relying upon a theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly

inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original). Again, the Examiner has failed to provide any basis in fact and/or technical reasoning.

For this reason, the Examiner has not met the burden of proof imposed by MPEP § 2112 and the burden has not shifted to Applicants. Therefore, the rejection is technically deficient and, as such, must be withdrawn.

The protein disclosed in Price does not bind HLA antigen nor is it recognized by CTL

In the interest of compact prosecution, however, Applicants respectfully submit that the protein disclosed by Price does not bind HLA antigen nor is it recognized by CTL. "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill in the art. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.'" In re Robertson, 169 F.3d 743, 745 (Fed. Cir. 1999) (citations omitted). Thus, in order for the protein of Price to inherently have the claimed function, it must

be established that (1) the claimed features of binding to HLA and being recognized by CTL are necessarily present, and (2) that ability of the protein of Price to bind HLA and be recognized by CTL would be recognized by one of ordinary skill in the art.

Regarding the first requirement, there is no evidence of record regarding Price, showing that the protein disclosed therein necessarily would bind HLA and be recognized by CTL. In fact, all evidence of record points to the opposite conclusion. Applicants submitted Boon, "Teaching the Immune System to Fight Cancer," *Scientific American*, March 1993 with the Reply under 37 C.F.R. § 1.111 filed on December 18, 2002. The Figure on page 36 of Boon shows that only the tumor antigen **peptides** (depicted with the red bars indicated as PEPTIDES) bind to HLA antigen (depicted with the green indicated as CLASS I MHC), are presented on the cell surface, and are recognized by CTL (depicted with T LYMPHOCYTE). The Figure also shows that the tumor antigen **protein** (depicted with the red coil indicated as PROTEIN) does not undergo this process. In the Office Action dated April 16, 2003, the Examiner does not respond to the reference of Boon. Thus, it is apparent that the evidence of record does not make clear that the missing descriptive matter (i.e., binding to HLA and being recognized by CTL) is necessarily present in the thing (i.e., protein) described in the of Price. In fact, the evidence of record clearly points away from this conclusion.

For the same reasons, the skilled artisan would not recognize that the protein of Price binds HLA and is recognized by CTL. Again, as noted above, the knowledge in the art (as evidenced by Boon) clearly teaches away from such a conclusion. As such, the skilled artisan would not even consider whether or not the protein could bind HLA and be recognized by CTL, since it is clearly established in the art not to have these functions. Since the second requirement of recognition is not met, inherency cannot be established.

Accordingly, the claimed peptide comprising an amino acid sequence that is a partial cyclophilin B sequence is clearly differentiated from the cyclophilin B protein. For these reasons, Price has not met every limitation of the claims. Further, the Examiner has failed to show that these missing limitations are inherently present in the protein of Price. Therefore, Price fails to anticipate the instant claims. Withdrawal of the instant rejection is respectfully requested.

Conclusion

Applicants respectfully submit that the above amendments and/or remarks overcome the rejections of record. The instant claims recite patentable subject matter such that the present application is in condition for allowance. The Examiner is

respectfully requested to issue a Notice of Allowability indicating that claims 2, 4, 6, 8, 10-12, and 25 are allowed.

If the Examiner has any questions concerning this application, the Examiner is requested to contact the Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at (703) 205-8000.

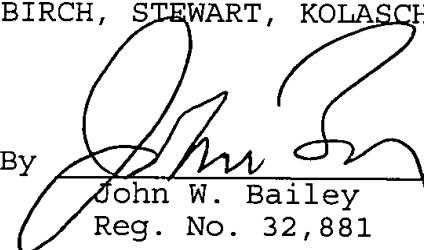
Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of two (2) months to September 16, 2003 in which to file a reply to the Office Action. The required fee of \$410.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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By



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Attachments: Form PTO-1449 (December 22, 2000)
Form PTO-1449 (June 21, 2002)